Supplementary Online Content

Glatt S, Jemec GB, Forman S, et al. Efficacy and safety of bimekizumab in moderate to severe hidradenitis suppurativa: a phase 2, double-blind, placebo-controlled randomized clinical trial. *JAMA Dermatol.* Published online August 18, 2021. doi:10.1001/jamadermatol.2021.2905

This supplementary material has been provided by the authors to give readers additional information about their work.

eMethods. Supplemental Methods

Concomitant Medications
Concomitant medications/treatments permitted during the study included antiseptic therapy, wound care, analgesic therapy (concomitant oral analgesics or opioid use within 14 days of baseline [excluding tramadol or stable doses of non-opioid analgesics] were not permitted), and antibiotic therapy. After baseline, permitted analgesics included ibuprofen, acetaminophen/paracetamol, or if pain was still uncontrolled, tramadol.

Rescue treatment was allowed (analgesics, abscess incision/drainage, intralesional triamcinolone injections) if a participant required emergency treatment for an uncontrolled flare (≥25% increase and an absolute increase in ≥2 in total abscess and inflammatory nodule count from baseline).

Additional sensitivity analysis sets
The randomized set consisted of all study participants randomized to the study, with the full analysis set (FAS) consisting of those who received at least one dose (full or partial) of investigational medicinal product and had a valid baseline measurement and a post-baseline measurement for at least one efficacy variable. The per-protocol set (PPS) included those participants who had no important protocol deviations affecting the primary efficacy variable.

Secondary sensitivity analyses of the primary outcome included a full analysis set (all randomization participants who received any quantity of study medication). Further sensitivity analyses excluded early treatment discontinuations (observed cases only). We performed a sensitivity analysis comparing bimekizumab and placebo using vague prior for both arms (equivalent to a frequentist analysis).

eResults. Supplementary Results

Sensitivity analyses
The primary efficacy analysis set was the per-protocol set; however, the primary analysis and all supportive and sensitivity analyses of the primary efficacy variables were repeated using the full analysis set and without applying non-responder imputation for missing response data (**eTable 2**).

Pharmacokinetics
Following the single subcutaneous loading dose of 640 mg, median serum bimekizumab trough concentration taken pre-dose at Week 2 was 25.6 µg/mL, which was lower than the expected 39.4 µg/mL based on previous studies of bimekizumab in psoriasis. Week 2 was selected based on the ease of comparison given the different dosing schedules and sampling schedules between studies.

The inflammatory burden in HS is greater than other auto-inflammatory conditions affecting the skin. Consistent with the recognition of the high inflammatory burden in HS, recent clinical studies of adalimumab in HS showed the need for higher induction and maintenance doses in HS compared with PSO (adalimumab European Public Assessment Report). Therefore, for bimekizumab, the dose required in HS subjects was expected to be higher than the maximum doses being explored for use in subjects with PSO and other indications under development.

eTable 1. Additional Bayesian analyses of HiSCR at Week 12 using informative prior distributions and NRI (FAS)

Posterior response rate		**Placebo**	**Bimekizumab**
N	Observed	19	42
	NRI	2	4
Mean (standard deviation)		25.5 (6.7)	54.6 (7.4)
Median		25.0	54.6
95% credible interval		13.5, 39.6	40.1, 68.8
Posterior difference from placebo (%)			
Mean (standard deviation)		29.1 (9.9)	
95% credible interval		9.2, 48.1	
Probability [Difference >0%] (%)		99.8	

The posterior difference from placebo is based upon 30000 posterior samples. The informative prior used for the placebo arm added 20 effective subjects. Results were based on a Bayesian logistic regression model where the number of responders was assumed to follow a binomial distribution; treatment and baseline Hurley Stage were included as predictors in the model; probability [Difference >0%] (%)=probability that the bimekizumab response rate was greater than the placebo response rate. HiSCR: Hidradenitis Suppurativa Clinical Response; NRI: non-responder imputation; FAS: full analysis set.

eTable 2. Bayesian analysis of HiSCR at Week 12 using vague prior distributions and NRI (PPS)

Posterior response rate		**Placebo**	**Bimekizumab**
N	Observed	18	40
	NRI	2	4
Mean (standard deviation)		25.6 (9.3)	57.3 (7.4)
Median		24.8	57.4
95% credible interval		9.8, 45.9	42.5, 71.6
Posterior difference from placebo (%)			
Mean (standard deviation)		31.7 (11.9)	
95% credible interval		7.0, 53.4	
Probability [Difference >0%] (%)		99.3	

The posterior difference from placebo is based upon 30000 posterior samples. Results were based on a Bayesian logistic regression model where the number of responders was assumed to follow a binomial distribution; treatment and Baseline Hurley Stage were included as predictors in the model; probability [Difference >0%] (%)=probability that the bimekizumab response rate was greater than the placebo response rate; patients with missing data at Week 12 (due to early discontinuation or other reason) were considered as non-responders for the analysis.
HiSCR: Hidradenitis Suppurativa Clinical Response; NRI: non-responder imputation; PPS: per-protocol set.

eTable 3. Bayesian analysis of HiSCR at Week 12 using vague prior distributions and NRI (FAS)

Posterior response rate		**Placebo**	**Bimekizumab**
N	Observed	19	42
	NRI	2	4
Mean (standard deviation)		24.5 (9.0)	54.6 (7.3)
Median		23.7	54.6
95% credible interval		9.3, 43.8	40.3, 68.7
Posterior difference from placebo (%)			
Mean (standard deviation)		30.2 (11.6)	
95% credible interval		6.3, 51.6	
Probability [Difference >0%] (%)		99.3	

The posterior difference from placebo is based upon 30000 posterior samples. Results were based on a Bayesian logistic regression model where the number of responders was assumed to follow a binomial distribution; treatment and Baseline Hurley Stage were included as predictors in the model; probability [Difference >0%] (%)=probability that the bimekizumab response rate was greater than the placebo response rate; patients with missing data at Week 12 (due to early discontinuation or other reason) were considered as non-responders for the analysis.
HiSCR: Hidradenitis Suppurativa Clinical Response; NRI: non-responder imputation; FAS: full analysis set.

eTable 4. Bayesian analysis of HiSCR at Week 12 using informative prior distributions and observed cases only (PPS)

Posterior response rate		**Placebo**	**Bimekizumab**
N	Observed	18	40
	NRI	n/a	n/a
Mean (standard deviation)		27.3 (7.2)	63.1 (7.7)
Median		26.9	63.3
95% credible interval		14.4, 42.3	47.6, 77.4
Posterior difference from placebo (%)			
Mean (standard deviation)		35.8 (10.5)	
95% credible interval		14.6, 55.6	
Probability [Difference >0%] (%)		99.9	

The posterior difference from placebo is based upon 30000 posterior samples. The informative prior used for the placebo arm added 20 effective subjects. Results were based on a Bayesian logistic regression model where the number of responders was assumed to follow a binomial distribution; treatment and Baseline Hurley Stage were included as predictors in the model; probability [Difference >0%] (%)=probability that the bimekizumab response rate was greater than the placebo response rate; patients with missing data at Week 12 (due to early discontinuation or other reason) were considered as non-responders for the analysis. HiSCR: Hidradenitis Suppurativa Clinical Response; NRI: non-responder imputation; PPS: per-protocol set.

eTable 5. Bayesian analysis of HiSCR at Week 12 using informative prior distributions and observed cases only (FAS)

Posterior response rate		**Placebo**	**Bimekizumab**
N	Observed	19	42
	NRI	n/a	n/a
Mean (standard deviation)		26.7 (7.1)	59.9 (7.6)
Median		26.3	60.0
95% credible interval		14.1, 41.7	44.5, 74.2
Posterior difference from placebo (%)			
Mean (standard deviation)		33.1 (10.3)	
95% credible interval		12.3, 52.6	
Probability [Difference >0%] (%)		99.9	

The posterior difference from placebo is based upon 30000 posterior samples. The informative prior used for the placebo arm added 20 effective subjects. Results were based on a Bayesian logistic regression model where the number of responders was assumed to follow a binomial distribution; treatment and Baseline Hurley Stage were included as predictors in the model; probability [Difference >0%] (%)=probability that the bimekizumab response rate was greater than the placebo response rate; patients with missing data at Week 12 (due to early discontinuation or other reason) were considered as non-responders for the analysis. HiSCR: Hidradenitis Suppurativa Clinical Response; NRI: non-responder imputation; FAS: full analysis set.

eTable 6. Observed case responders (PPS)

HiSCR						
n/N (%)	**Week 2**	**Week 4**	**Week 6**	**Week 8**	**Week 10**	**Week 12**
BKZ	16/44 (36)	22/44 (50)	29/43 (67)	28/42 (67)	31/42 (74)	25/40 (63)
PBO	3/20 (15)	6/19 (32)	4/19 (21)	4/19 (21)	4/18 (22)	5/18 (28)
ADA	8/20 (40)	8/20 (40)	11/19 (58)	10/19 (53)	10/19 (53)	12/18 (67)
$HiSCR_{75}$						
n/N (%)	**Week 2**	**Week 4**	**Week 6**	**Week 8**	**Week 10**	**Week 12**
BKZ	7/44 (16)	15/44 (34)	17/43 (40)	20/42 (48)	25/42 (60)	20/40 (50)
PBO	1/20 (5)	1/19 (5)	1/19 (5)	0	1/18 (5)	2/18 (11)
ADA	3/20 (15)	4/20 (20)	3/19 (16)	6/19 (32)	5/19 (26)	7/18 (39)
$HiSCR_{90}$						
n/N (%)	**Week 2**	**Week 4**	**Week 6**	**Week 8**	**Week 10**	**Week 12**
BKZ	5/44 (11)	12/44 (27)	15/43 (35)	15/42 (36)	17/42 (41)	14/40 (35)
PBO	0	0	0	0	0	0
ADA	3/20 (15)	1/20 (5)	3/19 (16)	3/19 (16)	3/19 (16)	3/18 (17)

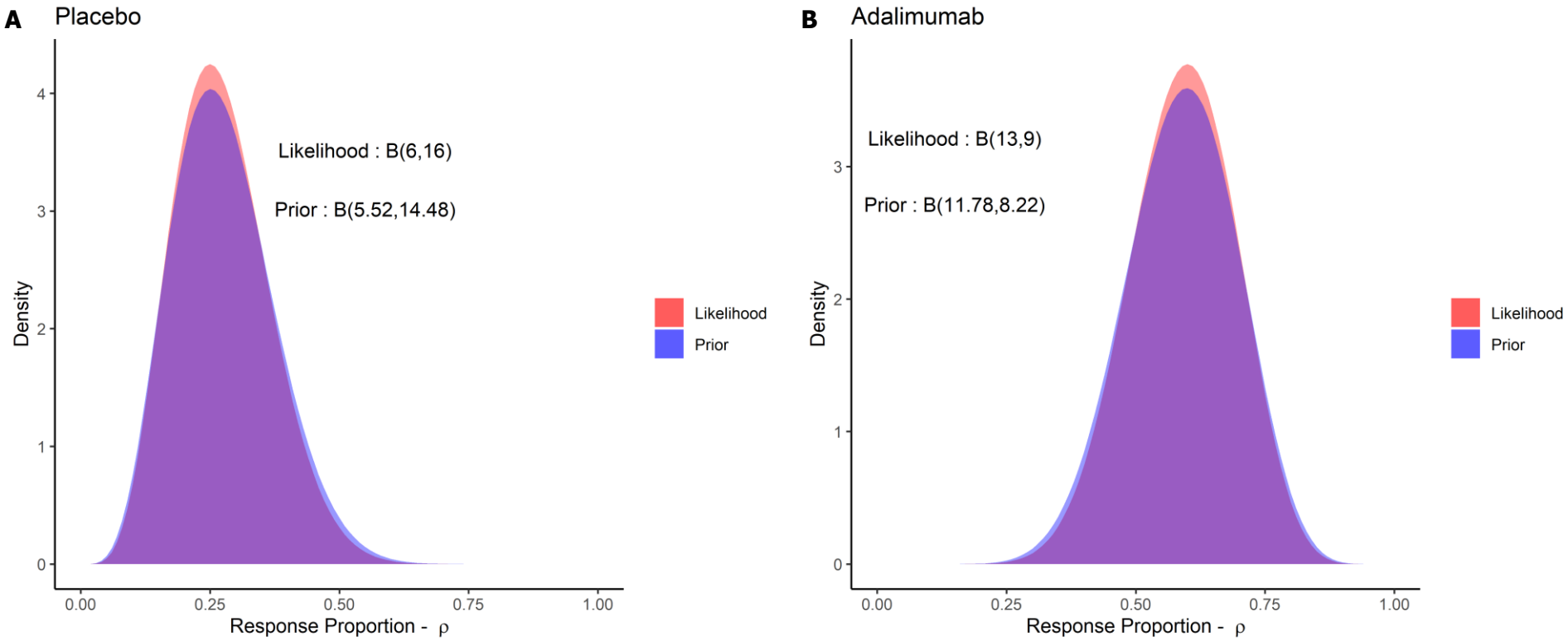
ADA: adalimumab; BKZ: bimekizumab; HiSCR: Hidradenitis Suppurativa Clinical Response; PBO: placebo; PPS: per-protocol set.

eTable 7. Rescue medication from Week 0–30 (through Safety Follow-Up)

Rescue Medication, n (%)[a]	Bimekizumab (n=46)	Placebo (n=21)	Adalimumab (n=21)	All participants (N=88)
Any rescue medication during the study	6 (13)	3 (14)	8 (38)	17 (19)
Anti-infectives for systemic use	3 (7)	2 (10)	6 (29)	11 (13)
Minocycline	0	1 (5)	1 (5)	2 (2)
Minocycline hydrochloride	1 (2)	0	0	1 (1)
PIP/Tazo	0	0	1 (5)	1 (1)
Spektramox	0	0	1 (5)	1 (1)
Sultamicillin	0	0	1 (5)	1 (1)
Cefalexin	1 (2)	0	0	1 (1)
Ceftriaxone sodium	0	0	1 (5)	1 (1)
Levofloxacin	0	1 (5)	1 (5)	2 (2)
Ciprofloxacin	1 (2)	0	0	1 (1)
Sulfamethoxazole	0	0	1 (5)	1 (1)
Trimethoprim	0	0	1 (5)	1 (1)
Doxycycline	0	0	1 (5)	1 (1)
Antineoplastic and immunomodulating agents	1 (2)	1 (5)	2 (10)	4 (5)
Adalimumab	1 (2)	1 (5)	2 (10)	4 (5)
Dermatologicals	1 (2)	0	0	1 (1)
Clindamycin phosphate	1 (2)	0	0	1 (1)
Musculoskeletal system	1 (2)	0	1 (5)	2 (2)
Ibuprofen	1 (2)	0	0	1 (1)
Ketorolac tromethamine	0	0	1 (5)	1 (1)
Nervous system	2 (4)	1 (5)	3 (14)	6 (7)
Tramadol	2 (4)	1 (5)	0	3 (3)
Hydrocodone	0	0	1 (5)	1 (1)
Hydromorphone	0	0	1 (5)	1 (1)
Morphine	0	0	1 (5)	1 (1)
Paracetamol	0	1 (5)	1 (5)	2 (2)
Systemic hormonal preparations, excluding sex hormones	1 (2)	0	2 (10)	3 (3)
Prednisone	0	0	1 (5)	1 (1)
Triamcinolone	0	0	1 (5)	1 (1)
Triamcinolone acetonide	1 (2)	0	0	1 (1)

[a] Unique rescue medications reported, some patients were treated with multiple rescue medications. Safety set (N=88), observed data. This summary included rescue medication as identified by medical review that started after the first dose through to the end of the Safety Follow-Up (Week 30); last dose of investigational medicinal product was given at Week 10.

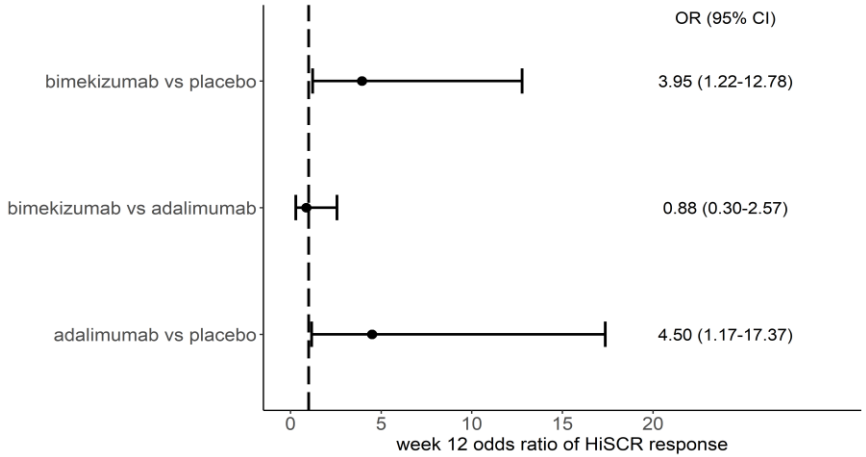
eFigure 1. Probability density functions for HiSCR response in primary analysis for placebo



eFigure 1: The prior and likelihood probability density functions for HiSCR response in the primary analysis for placebo (**A**) and adalimumab (**B**) treatment arms. The likelihood was calculated using $\beta(m+1, n+1-m)$, where m is the number of observed responders, and n is the number of subjects in the treatment group. HiSCR: Hidradenitis Suppurativa Clinical Response.

eFigure 2: Observed Cases Frequentist Analysis (FAS)

Treatment Arm	N	Responders	Non-responders	% Responders
Bimekizumab	44	25	19	56.8
Placebo	20	5	15	25.0
Adalimumab	20	12	8	60.0



eFigure 2: The lower limit of the 95% CI for the OR of HiSCR response between BKZ vs. PBO and ADA vs. PBO excludes 1; indicating a treatment superiority for BKZ and ADA as compared with PBO. By contrast, the CI of response between BKZ and ADA does not exclude 1 (i.e. no treatment difference in probability of response). ADA: adalimumab; BKZ: bimekizumab; CI: confidence interval; FAS: full analysis set; HiSCR: Hidradenitis Suppurativa Clinical Response; OR: odds ratio; PBO: placebo